Remarks

Reconsideration of this Application is respectfully requested.

Claims 1 and 3 are sought to be cancelled without prejudice to or disclaimer of the subject matter therein, claims 2, 4-8, 12, 13 and 15 are sought to be amended, and claims 41-56 are sought to be added. Upon entry of the foregoing amendment, claims 2, 4-16 and 41-56 are currently under consideration in the application, with claims 2 and 41 being the independent claims.

Support for the amendments to the claims can be found throughout the specification and in the claims as originally filed. Claim 2 was amended to be in independent form and to explicitly recite a limitation from cancelled claim 1. Claims 4-8 were amended to reflect proper claim dependency after cancellation of claim 1. Further support for claim 2 can be found, for example, in the specification at page 6, lines 1-4. Support for the amendment to claims 12 and 13 can be found in original claims 8 and 11. Support for the amendment to claim 15 can be found, for example, in the specification at page 11, lines 9-13. Support for new claims 41- 54 can be found in claims 3-16 as filed. Support for new claims 55 and 56 can be found, for example, in the specification at page 10, lines 7-20 and page 20, line 20 to page 21, line 17. These changes are believed to introduce no new matter, and their entry is respectfully requested.

Based on the above amendment and the following remarks, Applicants respectfully request that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Election/Restrictions

The Examiner acknowledged Applicants' election with traverse of Group I (claims 1-16). (*See* Paper No. 16, page 2.) Since it was the Examiner's view that Applicants' arguments were not persuasive, the Examiner deemed the requirement proper and therefore made it final. (*See id.*) The Examiner also indicated that claims 17-40 were withdrawn from consideration, thereby indicating that claims 1-16 were under consideration. (*See id.*) In addition, the Examiner indicated that "Applicant's request for further examination of groups VII [sic] upon allowability of the product of group I has been considered and is accepted." (Paper No. 16, page 2.)

Drawings

The Examiner objected to the drawings of Figures 1A-1C "because there is no description of these drawings in the 'Brief Description of the Drawings' section." (Paper No. 16, page 2.) The Examiner further indicated that a proposed drawing correction or corrected drawings were required in the Reply to the Office Action to avoid abandonment, and that the objection would not be held in abeyance. (*See id.*)

In response to the Examiner's objection, Applicants have amended the "Brief Description of the Drawings" section of the specification to reflect the different subparts of Figure 1, thereby rendering the objection moot. A more detailed discussion of Figures 1A-1C can be found in Example 1, pages 27-29.

Rejections under 35 U.S.C. § 112, Second Paragraph

The Examiner rejected claim 15 under 35 U.S.C. § 112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. (*See* Paper No. 16, page 3.)

Specifically, the Examiner contends that "[c]laim 15 states that the foreign DNA is a tumor antigen or a 'fragment thereof'. The metes and bounds of what is considered a 'fragment thereof' has not been described." (Paper No. 16, page 3.) Applicants respectfully traverse this rejection.

The definiteness requirement "requires the language of the claim to set forth clearly the domain over which the applicant seeks exclusive rights." *Process Control Corp. v. HydReclaim Corp.*, 190 F.3d 1350,1358 n.2, 52 USPQ2d 1029, 1034 n.2 (Fed. Cir. 1999). Further, "[t]he test for whether a claim meets the definiteness requirement is 'whether one skilled in the art would understand the bounds of the claim when read in light of the specification.'" *Process Control*, 190 F.3d at 1358 n.2, 52 USPQ2d at 1034 n.2 (quoting *Personalized Media Communications v. Int'l Trade Comm'n,* 161 F.3d 696, 705, 48 USPQ2d 1880, 1888 (Fed. Cir. 1998)). "If the claims read in light of the specification reasonably apprise those skilled in the art of the scope of the invention, § 112 demands no more." *Miles Laboratories, Inc. v. Shandon Inc.,* 997 F.2d 870, 875 (Fed. Cir. 1993), *cert. denied*, 510 U.S. 1100 (1994) (citations omitted). Applicants submit that claim 15, when read in light of the specification, reasonably apprises one skilled in the art of the metes and bounds of the claimed invention.

As disclosed in the specification, "[e]xamples for human vaccine applications, gene therapy and tumor vaccine applications are given in WO 97/40180, which is fully

incorporated by reference herewith." (Specification, page 16, lines 12-14.) "With regard to the production of cellular tumour vaccines or for pharmaceutical compositions with which the immune response to tumours is to be intensified," WO 97/40180 discloses that "the foreign DNA codes for immunostimulating proteins or tumour antigens or fragments thereof." (English Translation of WO 97/40180, page 12, lines 9-13.) In addition, it is disclosed in the specification that "[f]or vaccine applications, the foreign DNA encodes one or more antigens eliciting an immune response in the individual. The antigen may be the natural protein derived from the pathogen, or an immunogenic fragment thereof, e.g. an immunogenic peptide." (Specification, page 11, lines 9-13.)

Claim 15, as amended, is directed to recombinant CELO virus or CELO virus DNA characterized in that the foreign DNA encodes a tumor antigen or an *immunogenic* fragment thereof. As such, one skilled in the art would clearly understand that the fragment of the tumor antigen is one that induces an immune response in the individual. Based on the disclosure, as well as the amendment to claim 15, the scope of this claim would be reasonably ascertainable by those skilled in the art.

The Examiner's grounds of rejection of claim 15 under 35 U.S.C. § 112, second paragraph, have been addressed by Applicants' amendments and/or remarks. Accordingly, the Examiner is respectfully requested to reconsider and withdraw this rejection.

Double Patenting

The Examiner rejected claims 1-16 under the judicially created doctrine of obviousness-type double patenting as allegedly being unpatentable over claims 1, 4, 5, 8, 16, 20-28, 30-34, 81, 83 and 149-162 of U.S. Patent No. 6,335,016 ("the '016 patent"). (*See*

Paper No. 16, page 3.) In particular, the Examiner asserted that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the mutated regions in the patent are overlapping with the regions in the instant application." (Paper No. 16, page 3.)

Applicants respectfully disagree with the Examiner's assertion. However, solely in an effort to facilitate prosecution, Applicants will file a terminal disclaimer in compliance with 37 C.F.R. § 321 upon allowance of the claims of the present invention.

Rejections under 35 U.S.C. § 102

The Examiner rejected claims 1-5, 7 and 8 under 35 U.S.C. § 102(a) as allegedly being anticipated by Michou *et al.*, *Journal of Virology 73*:1399-1410 (1999). (*See* Paper No. 16, page 4.) In particular, the Examiner asserted that

> Michou et al. teaches recombinant CELO genome construct, pAIM45, that has nt deletions spanning 33358-43684 and expresses the luciferase gene in place of the deleted sequences, see Table 2 on page 1401 and Figure 3 on page 1403. The construct is expressed on a plasmid that replicates in *E. coli*, see the see the [sic] second column on page 1402. Although Michou et al. does not expressly teach that Gam1 expression is inhibited in the construct, this feature would be an inherent characteristic since the region spanning Gam1 expression is deleted.

(Paper No. 16, pages 4-5.)

The Examiner also rejected claims 1-16 under 35 U.S.C. § 102(b) as allegedly being anticipated by Baker *et al.*, International Publication No. WO 97/40180. (*See* Paper No. 16, page 5.) Specifically, the Examiner asserted that

> Baker et al. teaches a CELO virus deleted between nucleotides 31,800 - 43,734 and 794 - 1330, which are

> suitable site for foreign DNA insertion. The foreign DNA encodes for an animal pathogen, an avian pathogen, a human protein, a therapeutically active protein, an immunostimulatory protein, a cytokine, a human pathogen, or a tumor antigen, see claims 1-13, and 16. The CELO virus of Baker et al. expressed by a plasmid which is replicable in bacteria, yeast, or bird embryo kidney or liver cell lines, see page 11, lines 15-19.

(Paper No. 16, page 5.)

The Examiner further rejected claims 1-16 under 35 U.S.C. § 102(e) as allegedly being anticipated by Baker *et al.*, U.S. Patent No. 6,335,016.[1] (*See* Paper No. 16, page 5.) Particularly, it is the Examiner's position that

> Baker et al. teaches a CELO virus deleted between nucleotides 31,800 - 43,734 and 794 - 1330, which are suitable site for foreign DNA insertion. The foreign DNA encodes for an animal pathogen, an avian pathogen, a human protein, a therapeutically active protein, an immunostimulatory protein, a cytokine, a human pathogen, or a tumor antigen, see claims 1, 4, 5, 8, 16, 20-28, 30-34, 81, 83, and 149-162. The CELO virus of Baker et al. expressed by a plasmid which is replicable in bacteria, yeast, or bird embryo kidney or liver cell lines, see column 6, lines 3-7.

(Paper No. 16, pages 5-6.) Applicants respectfully submit that the above cited references do not anticipate the claimed invention.

Anticipation of a claim under § 102 can be found only if the prior art reference discloses each and every element as set forth in the claim. *See Glaxo Inc. v. Novopharm Ltd.*, 34 USPQ2d 1565, 1567 (Fed. Cir. 1995), *cert denied,* 116 S. Ct. 516 (1995). While Michou *et al.* generally teach a deletion of nucleotides 33,358 - 43,684 of the wild-type

---

[1]Applicants note that U.S. Patent No. 6,335,016 issued from U.S. Application No. 09/171,461, which is the U.S. National Stage application of PCT/EP97/01944, *i.e.*, International Publication No. WO 97/40180. Accordingly, the '016 patent and WO 97/40180 share the same specification, and the discussion of WO 97/40180 is likewise applicable to the '016 patent.

CELO genome, the reference does not specifically teach modifications in the claimed regions which negatively effect Gam1 protein expression, *i.e.*, nucleotides 37,391 - 38,239 and 36,818 - 37,972.

Similarly, WO 97/40180 generally discloses that the section in the CELO virus genome from about nucleotide 31,000 to about 43,804 includes sequences which code for a protein or an RNA molecule which is necessary for the interaction with the host cell machinery or with the host immune system and that these proteins should be required in fairly low concentrations or may be dispensable for cultivation of the virus in the tissue culture. (*See* English Translation of WO 97/40180, page 21, lines 12-18.) WO 97/40180 further discloses that modifications of the CELO virus genome can be performed on a section of the CELO virus DNA which includes the nucleotides from about 31,800 to about 43,734, *i.e.,* the section at the right hand end located in front of the right terminal repeat. (*See* English Translation of WO 97/40180, page 10, lines 19-27.)

The Examiner asserted that the claimed invention is "clearly anticipated" by the teachings of Michou *et al.*, WO 97/40180 and the '016 patent. (Paper No. 16, pages 4-5.) However, Applicants respectfully submit that the Examiner has not provided any support for this proposition, *i.e.*, that the scope of deletions in the CELO virus of these references encompasses and anticipates any range of nucleotide deletions within the range taught.

While the presently claimed species of modified CELO virus or CELO virus DNA is arguably *encompassed* by the genus disclosed in these references, it is not *anticipated* by them. Although Michou *et al.*, WO 97/40180, the '016 patent and Applicants disclose a CELO virus or CELO virus DNA which contains deletions in the right-end of the CELO virus genome, the disclosure of a genus *does not necessarily anticipate* a species within that

genus. *See Corning Glass Works v. Sumitomo Electric U.S.A., Inc.* 9 USPQ2d 1962, 1970 (Fed. Cir. 1989); *see also In re Meyer*, 202 USPQ 175, 179 (CCPA 1979) (prior art genus "alkaline chlorine or bromine solution" does not identically disclose or describe, within the meaning of §102, the claimed species "alkali metal hypochlorite" since the genus would include an untold number of species). Anticipation of a claim under § 102 can be found only if the prior art reference discloses each and every element as set forth in the claim. *See Glaxo Inc. v. Novopharm Ltd.*, 34 USPQ2d 1565, 1567 (Fed. Cir. 1995), *cert denied,* 116 S. Ct. 516 (1995). Further, "[t]he identical invention must be shown in as complete detail as is contained in the . . . claim." *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989). Applicants submit that the cited references do not disclose the invention in as complete detail as the *claimed invention.*

Applicants' claimed invention discloses a recombinant CELO virus or CELO virus DNA wherein the regions spanning nucleotides 37,391 - 38,239 and 36,818 - 37,972 of the wild-type CELO virus genome are completely or partially deleted and/or contain an insertion of foreign DNA. Michou *et al.* generally describe a CELO virus characterized in that it contains modifications which are located on a section of the CELO virus DNA which comprises the nucleotides from 33,358 - 43,684, and WO 97/40180 generally describes a CELO virus characterized in that it contains modifications which are located on a section of the CELO virus DNA which comprises the nucleotides from about 31,800 to about 43,734. "[A]lthough . . . specific claims are subsumed in [a prior art reference's] generalized disclosure . . ., this is not literal identity." *Minnesota Mining & Mfg. Co. v. Johnson & Johnson Orthopaedics, Inc.*, 24 USPQ2d 1321, 1332 (Fed. Cir. 1992). As such, in failing to expressly disclose the specific nucleotide regions identified in the present

application which can be modified such that a complete loss of Gam1 expression or prevention of the expression of a functional Gam1 protein occurs, *i.e.*, 37,391 - 38,239 and 36,818 - 37,972, Michou *et al.*, WO 97/40180 and the '016 patent do not contain each and every element as set forth in Applicants' claims.

When a claimed compound is not specifically named in a prior art reference, but instead it is necessary to select various substituents from a list of alternatives, anticipation can only be found if the classes of substituents are sufficiently limited or well delineated. *See, e.g., Ex parte A*, 17 USPQ2d 1716, 1718 (BPAI 1990). That is, a genus will anticipate a species within that genus which is not expressly disclosed if one of ordinary skill would "at once envisage" the claimed compound from the disclosed genus. *See In re Petering*, 133 USPQ 275, 280 (CCPA 1962).

Other than the disclosure of a CELO mutant which lacks the sequences from nucleotides 35,870 to 42,373 at the right hand end of the virus genome, WO 97/40180 and the '016 patent do not attempt to limit the genus of compounds, but rather describe the genus broadly as including CELO virus that contains modifications located on a section of the CELO virus DNA comprising nucleotides from about 31,800 to about 43,734. Since this region contains almost 12,000 nucleotides and any or all of the nucleotides within the region can be deleted, Applicants submit that one skilled in the art, given only the disclosure of these references, could not "at once envisage" Applicants' presently claimed compounds in view of the vast number of possible deletions. Likewise, since the region of Michou *et al.* contains over 10,000 nucleotides, Applicants submit that the skilled artisan, given only the disclosure of Michou *et al.*, could not "at once envisage" Applicants' presently claimed compounds.

The Examiner also asserted that "[a]lthough the conflicting claims are not identical, they are not patentably distinct from each other because the mutated regions in the ['016] patent are overlapping with the regions in the instant application." (Paper No. 16, page 3.) Even if the Examiner interprets the references as disclosing a "range" of deletions, the M.P.E.P. indicates that

> [w]hen the prior art discloses a range which touches, overlaps or is within the claimed range, but no specific examples falling within the claimed range are disclosed, a case by case determination must be made as to anticipation. In order to anticipate the claims, the claimed subject matter must be disclosed in the reference with "sufficient specificity to constitute an anticipation under the statute." What constitutes a "sufficient specificity" is fact dependent. If the claims are directed to a narrow range, the reference teaches a broad range, and there is evidence of unexpected results within the claimed narrow range, depending on the other facts of the case, it may be reasonable to conclude that the narrow range is not disclosed with "sufficient specificity" to constitute an anticipation of the claims. . . . The question of "sufficient specificity" is similar to that of "clearly envisaging" a species from a generic teaching.

M.P.E.P. § 2131.03 at 2100-57. Applicants submit that the cited references do not disclose the claimed invention with sufficient specificity to constitute an anticipation.

The specification discloses that

> The present invention relates to recombinant CELO virus or CELO virus DNA that have the region spanning nucleotides 37391-38239 of the CELO wild type virus genome completely or partially deleted or altered or that contain an insertion in this region, any of which modifications results in a complete loss of Gam1 expression or prevents the expression of a functional Gam1 protein.

(Specification, page 5, lines 3-10.)

Moreover, the specification discloses that

> [t]he disruption in the Gam1 gene renders CELO AIM65 extensively defective in replication. A study of the biological function of the Gam1 gene revealed that Gam1 expression leads to increases in the cellular levels of certain heat shock proteins. It was therefore hypothesized that an essential function of Gam1 is to upregulate a heat shock response during infection. Based on this hypothesis, it was tested whether heat shock applied to the infected cell could allow the replication of a CELO derivative lacking the Gam1 gene. Surprisingly it was found that, although the Gam1 deletion severely impaired CELO virus replication, the functions of the Gam1 gene in virus replication could be provided by exposing the host cells to a heat shock. This novel type of complementation allows to grow viruses that otherwise are severely defective in their replication capacity.

(Specification, page 9, lines 20-29.)

The claimed invention is arguably directed to a narrow range of CELO virus alterations, whereas the cited references arguably teach a broad range. In addition, as demonstrated above, there is evidence of unexpected results within the claimed narrow range. Consequently, Applicants submit that it is be reasonable to conclude that the narrow range is not disclosed with "sufficient specificity" to constitute an anticipation of the claims.

In view of the fact that the cited references fail to expressly set forth any of Applicants' claimed regions, that one skilled in the art would be unable to immediately envisage Applicants' claimed regions from the disclosed genuses, and the references do not disclose the claimed invention with sufficient specificity, it is clear that the present invention is not anticipated by Michou *et al.*, WO 97/40180 or the '016 patent. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C. § 102 be withdrawn.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicants therefore respectfully request that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Peter A. Jackman
Attorney for Applicants
Registration No. 45,986

Date: August 12, 2002

1100 New York Avenue, N.W.
Suite 600
Washington, D.C. 20005-3934
(202) 371-2600

Version with Markings to Show Changes Made

In the Specification:

The paragraph on beginning on page 19, line 27 was substituted with the following paragraph:

Figures 1A-1C [Figure 1]. Demonstration that Gam1 expression elevates heat shock protein levels.

In the Claims:

Claims 1 and 3 have been cancelled without prejudice to or disclaimer of the subject matter contained therein.

Claims 2, 4-8, 12, 13 and 15 were amended as follows:

2. (Once amended) Recombinant [The recombinant] CELO virus or CELO virus DNA [of claim 1], characterized in that the region spanning nucleotides [nt] 37391-38239 of the CELO wild type virus genome is completely or partially deleted or altered and/or contains an insertion, wherein said deletion, alteration or insertion results in a complete loss of Gam1 expression or prevents the expression of a functional Gam1 protein.

4. (Once amended) The recombinant CELO virus or CELO virus DNA of claim 2 [claim 1], characterized in that it contains a modification in the Gam1 transcriptional control sequences.

5. (Once amended) The recombinant CELO virus or CELO virus DNA of claim 2 [claim 1], characterized in that it further contains a deletion of or within a region selected from the regions spanning nucleotides [nt] 41731-43684, nucleotides [nt] 41523-43684, nucleotides [nt] 41002-43684 and nucleotides [nt] 40065-43684.

6. (Once amended) The recombinant CELO virus or CELO virus DNA of claim 2 [claim 1], characterized in that it further contains a deletion spanning nucleotides [nt] 794-1330.

7. (Once amended) The recombinant CELO virus DNA of claim 2 [claim 1] contained on a plasmid that can be replicated in procaryotic or eucaryotic cells.

8. (Once amended) The recombinant CELO virus or CELO virus DNA of claim 2 [claim 1], characterized in that it contains a foreign DNA insertion in place of one or more deletions.

12. (Once amended) The recombinant CELO virus or CELO virus DNA of claim 11, characterized in that the foreign DNA encodes a therapeutically active protein.

13. (Once amended) The recombinant CELO virus or CELO virus DNA of claim 12, characterized in the foreign DNA encodes an immunostimulatory protein.

15. (Once amended) The recombinant CELO virus or CELO virus DNA of claim 11, characterized in that the foreign DNA encodes a tumor antigen or an immunogenic [a] fragment thereof.

Claims 41-56 were added.